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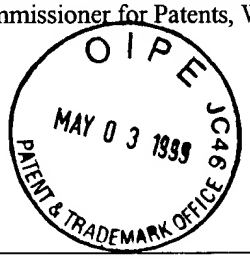


W. Scott McNees
(Print Name)

Date: April 29, 1999

W. Scott McNees
(Signature)

CASE DOCKET 9397

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

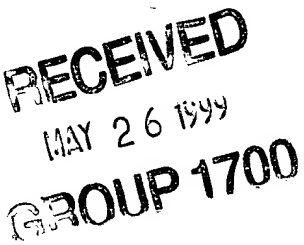
In re Patent Application of

Russell G. Higuchi — Group: 1743

Serial No. 08/968,208 filed November 12, 1997 — Examiner: J. Snay

For: **HOMOGENEOUS METHODS FOR NUCLEIC ACID AMPLIFICATION AND DETECTION**

RESPONSE TO OFFICE ACTION



BOX: Fee Amendment
Assistant Commissioner for Patents
Washington DC 20231

Sir:

This Response is submitted in reply to the Office Action dated October 30, 1998 in the above-captioned application. Claims 24-29 are pending.

In the Office Action, the Examiner rejected claims 23, 24, 27, and 28 under 35 U.S.C. 102(b) as allegedly anticipated by Hearst, et al. The Examiner stated that Hearst disclose a thermal cycler which further supports optics for fluorescence analysis, including a support for a plurality of amplification reaction volumes, reaction vessels and the optical system being coupled to the reaction vessels.

Applicant respectfully traverses this rejection. The claimed invention is directed to an instrument which comprises a thermal cycler and an optical system. The function of the thermal cycler, as is described in detail in the specification, is to repeatedly increase and decrease temperature through a broad range. The purpose of this cycling of high and low temperature is to alternately induce denaturation of nucleic acid at higher temperature, and synthesis of nucleic acid at lower temperature. The thermal cycler raises the temperature of the reaction vessels contained therein to a very high temperature at which nucleic acid denaturation occurs. The cycler then lowers the temperature of the reaction vessels to allow primer extension and synthesis of a new nucleic acid strand to take place.

The device disclosed in Hearst is designed to perform an opposite function with respect to temperature control. The Hearst device does not comprise a thermal cycler. On the contrary, Hearst discloses a mechanism for maintaining, rather than changing, the temperature of the reaction vessels. Hearst generally describes a device for use in photoactivation of photoreactive compounds. It is specifically stated that temperature change during the reaction process adversely affects the result and is undesirable (see column 90, lines 42-46). Hearst provides comparative examples of reactions performed with and without temperature maintenance (see column 90, lines 47-48, and Figures 15A and 15B), to demonstrate the advantage provided by the device which maintains a consistent temperature. The device of Hearst is specifically designed to maintain temperature, and not to change temperature, as is applicant's invention, and does not comprise a thermal cycler, as does applicant's claimed instrument.

Hearst does refer to thermal cycling in connection with nucleic acid amplification reactions. However, this is a separate operation from the photoactivation described, and the thermal cycler is a separate component and is used independently of the Hearst photoactivation device.

With respect to optical systems, the Hearst device is also different from applicant's invention. The presently claimed instrument comprises an optical system to enable monitoring of an amplification reaction. In one embodiment, the optical system may be a fluorometer. The primary purpose of the optical system is to monitor or detect light emission which results from a reaction.

The device disclosed in Hearst is not adapted to detect or monitor light which results from a reaction. As noted above, Hearst is generally concerned with causing photoactivation of photoreactive compounds. Consequently, the device comprises a light source for the purpose of causing a photoreaction to take place. The light source is provided specifically to irradiate the photoreactive compounds. This is distinctly different from the optical system in applicant's claimed instrument which detects light, rather than functioning as a source of irradiation.

The Examiner rejected claims 25, 26, and 29 under 35 103(a) as allegedly unpatentable over Hearst in view of Mackay. The Examiner noted that Hearst differs from applicant's invention by lacking optical fibers for conducting excitation or emitted light. The Examiner stated that the use of such optical fibers for fluorescence analysis of individual reaction volumes was well known, as shown by Mackay. The Examiner took the position that it would have been obvious to modify the apparatus of Hearst to include optical fibers for light transmission, to obtain the allegedly expected benefit of enhanced control of light transmission to and from individual reaction vessels.

Applicant has hereinabove set forth the distinctions between the claimed invention and the disclosure of Hearst. Mackay discloses the use of optical fiber for fluorescence analysis. However, Mackay does not teach or suggest the elements which are lacking from Hearst. Specifically, the combination of Mackay with Hearst lacks a thermal cycler. Furthermore, since

the fundamental function and device of Hearst are contrary to the claimed invention, the combination of Hearst and Mackay would teach away from the claimed invention. A device in accordance with the combined teachings of Hearst and Mackay would have a component for maintaining temperature, rather than repeatedly changing temperature.

With regard to the optical systems, Hearst is dedicated to photoactivation, and is not concerned with detection or monitoring light emission. As described in Hearst, the photoactivation is achieved by the use of multiple large light sources (see for example, Fig. 6, and column 85, line 61 - column 86, line 4, showing six light bulbs) which are required to provide for the large intensity of irradiation required for photoactivation. The optical fibers of Mackay simply provides minimal light to cause a fluorescent dye to emit a detectable signal. Thus, there is no motivation to combine the references, because the fiber optics of Mackay would not to provide the photoactivation capability required by Hearst.

For the reasons set forth above, applicants maintain that the claimed invention is neither anticipated by Hearst nor obvious in view of the combination of Hearst and Mackay. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw the rejections set forth in the October 30, 1998 Office Action.

Applicant acknowledges the objection to the drawings set forth in the Notice of Draftperson's Patent Drawing Review accompanying the Office Action. Applicant will submit formal drawings upon indication of allowable subject matter.

No fee, other than the accompanying fee for Petition of Extension of Time, is due. Authorization is given to charge the amount of any additional fee or credit any overpayment to Deposit Account No. 50-0812

If a telephone interview would advance prosecution of the subject application, the Examiner is invited to contact the undersigned attorney at the number provided.

Respectfully submitted,

Date: April 29, 1999

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